UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,682	10/16/2001	Barney Scott Graham	VBLT:003US/SLH	6636

7590 04/09/2003

FULBRIGHT & JAWORSKI L.L.P.
A REGISTERED LIMITED PARTNERSHIP
SUITE 2400
600 CONGRESS AVENUE
AUSTIN, TX 78701

EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/981,682	Applicant(s) GRAHAM ET AL.	
	Examiner Shaojia A. Jiang	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *10,12 and 21-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

The provisional application 60/241,247 upon which priority is claimed, appears to provide adequate support under 35 U.S.C. 112 for the elected invention of Group I claims 1-20 of this application (see Restriction Requirement in the Paper No. 10 and discussed further below).

Election/Restrictions

Applicant's election *without* traverse of the invention of Group I, Claims 1-20, and the invention of species of respiratory syncytial virus (RSV) as a single virus to be treated, in Paper No. 11, submitted February 3, 2003 is acknowledged.

Therefore, claims 21-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 10 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species.

The claims have been examined insofar as they read on the elected specie.

Claims 1-9, 11 and 13-20 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11 and 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "a subject" in claim 1 renders claims 1-9, 11 and 13-20 indefinite. The expression "a subject" is not seen to be defined in the specification. Hence, one of ordinary skill in the art could not interpret as to what is a subject herein, e.g., a cell, a mammal or an animal in the claim. Thus, the scope of the claims is indefinite.

The expression "severe combined immunodeficiency" in claim 4 renders claim 4 indefinite since the term "severe" is a relative term. The expression "severe combined immunodeficiency" is not seen to be defined in the specification. Hence, one of ordinary skill in the art could not interpret as to what is the subject suffers from "severe combined immunodeficiency" in the claim. Thus, the scope of the claims is indefinite.

The expression "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" in claim 14 renders claim 14 indefinite. The expression "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" is not seen to be clearly defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to the recitation "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" in the claim. Therefore, the scope of the claims is indefinite as to what would be considered "an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor" encompassed thereby.

The expression "a nucleoside analog composition" in claim 15 renders claim 15 indefinite. The expression "a nucleoside analog composition" is not seen to be clearly

defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to the recitation "a nucleoside analog composition" in the claim. Therefore, the scope of the claims is indefinite as to what would be considered "a nucleoside analog composition" encompassed thereby.

The expression "a protease inhibitor" in claim 16 renders claim 16 indefinite. The expression " a protease inhibitor " is not seen to be clearly defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to the recitation " a protease inhibitor " in the claim. Therefore, the scope of the claims is indefinite as to what would be considered "a protease inhibitor" encompassed thereby.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Maziere et al. (C24, PTO-1229 submitted June 11, 2002).

Maziere et al. teaches that HMG-CoA reductase inhibitors, such as lovastatin, are useful in a method of inhibiting HIV infective cycle in AIDS patients since lovastatin inhibits HIV-1 expression in H9 human T lymphocytes. See in Maziere et al., the title, "Summary", and page 66 "Conclusion". Maziere's method inherently treats or inhibits

infection of a cell by a virus in a subject such as a cell in *vitro*. Thus, Maziere et al. anticipates claims 1 and 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 11, 13, 15-16, and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1229 submitted June 11, 2002) and Park et al. (C29, PTO-1229 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1229 submitted June 11, 2002).

Maziere et al. teaches that HMG-CoA reductase inhibitors, such as lovastatin, are useful in a method of inhibiting HIV infective cycle in AIDS patients since lovastatin inhibits HIV-1 expression in H9 human T lymphocytes. See in Maziere et al., the title, "Summary", and page 66 "Conclusion". Maziere et al. also teaches that the particular nucleoside analog, AZT, is known to be useful in treating viral infection by inhibiting viral replication in humans. See "Introduction" page 63 the left column.

Park et al. teaches that HMG-CoA reductase inhibitors such as simvastatin and astrovastatin are useful in inhibiting of geranylgeranylation of RhoA GTPase. See pages 1-2.

The above cited prior art does not expressly disclose the employment of HMG-CoA reductase inhibitors in a method of inhibiting infection of a cell by a virus such as respiratory syncytial virus (RSV) in a human, a non-human mammal, or a livestock animal. The above cited prior art does also not expressly disclose the employment of HMG-CoA reductase inhibitors in combination with a nucleoside analog composition in a method of inhibiting infection of a cell by a virus such as respiratory syncytial virus (RSV).

Pastey et al. teaches that the interaction between the fusion protein of RSV and RhoA, a small GTPase, facilitates virus-induced syncytium formation and that RhoA-derived peptide inhibits RSV. See abstract and entire article, especially page 7262 and "Discussion" at page 7266-7269.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ HMG-CoA reductase inhibitors in a method of inhibiting infection of a cell by a virus such as RSV in a human, a non-human mammal, or a livestock animal, and to employ a HMG-CoA reductase inhibitor in combination with a nucleoside analog composition in a method of inhibiting infection of a cell by a virus such as RSV.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ HMG-CoA reductase inhibitors in a method of inhibiting infection of a cell by a virus such as RSV in a human, a non-human mammal, or a livestock animal, since HMG-CoA reductase inhibitors are known to be useful in a method for inhibiting infection of a cell by a virus such as HIV according to Maziere et al.

Moreover, Park et al. teaches that HMG-CoA reductase inhibitors such as simvastatin and astrovastatin are useful in inhibiting of geranylgeranylation of RhoA GTPase. It is also known that the inhibition of RhoA GTPase would result in inhibiting RSV according to Pastey et al. Therefore, one of ordinary skill in the art would have reasonably expected that HMG-CoA reductase inhibitors would have a beneficial therapeutic effect in inhibiting infection of a cell by a virus such as RSV in a subject such as in a human, a non-human mammal, or a livestock animal.

Additionally, one having ordinary skill in the art at the time the invention was made would have been motivated to employ a HMG-CoA reductase inhibitor in combination with a nucleoside analog composition in a method of inhibiting infection of a cell by a virus such as RSV, since the particular nucleoside analog, AZT composition, is known to be useful in treating viral infection by inhibiting viral replication in humans. Therefore, one of ordinary skill in the art would have reasonably expected that combining a HMG-CoA reductase inhibitor and AZT known useful for the same purpose, i.e., inhibiting a viral infection such as RSV, in a composition to be administered would improve the therapeutic effect for treating a viral infection such as RSV. Since all active composition components herein are known to useful to treat a viral infection such as RSV, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1229 submitted June 11, 2002) and Park et al. (C29, PTO-1229 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1229 submitted June 11, 2002) .

The same teachings of Maziere et al. have been discussed above 103(a) rejection (see supra at page 5 of the instant Office Action).

The same teachings of Park et al. have been discussed above 103(a) rejection (see supra at page 5 of the instant Office Action).

The same teachings of Pastey et al. have been discussed above 103(a) rejection (see supra at page 6 of the instant Office Action).

The above cited prior art does not expressly disclose the employment of HMG-CoA reductase inhibitors in combination with an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor in a method of inhibiting infection of a cell by a virus such as RSV.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a HMG-CoA reductase inhibitor in combination with an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor in a method of inhibiting infection of a cell by a virus such as RSV.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a HMG-CoA reductase inhibitor in combination with an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor, since a HMG-CoA reductase inhibitor and an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor are known to have same usefulness in inhibiting of geranylgeranylation of RhoA GTPase. As a result, they are useful in inhibiting RSV. Therefore, one of ordinary skill in the art would have reasonably expected that combining a HMG-CoA reductase inhibitor and an inhibitor of isoprenylation that is distinct from said HMG-CoA reductase inhibitor, known useful for the same purpose, i.e., inhibiting a viral infection such as RSV, in a composition to be administered would improve the therapeutic effect for treating a viral infection such as RSV. Since all active composition components herein are known to useful to treat a viral infection such as RSV, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1229 submitted June 11, 2002) and Park et al. (C29, PTO-1229

submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1229 submitted June 11, 2002) and Fisher et al. (C11, PTO-1229 submitted June 11, 2002)

The same teachings of Maziere et al. have been discussed above 103(a) rejection (see supra at page 5 of the instant Office Action).

The same teachings of Park et al. have been discussed above 103(a) rejection (see supra at page 5 of the instant Office Action).

The same teachings of Pastey et al. have been discussed above 103(a) rejection (see supra at page 6 of the instant Office Action).

The above cited prior art does not expressly disclose the employment of HMG-CoA reductase inhibitors in combination with an antibody composition in a method of inhibiting infection of a cell by a virus such as RSV.

Fisher et al. teaches that antibody compositions including monoclonal antibody and polyclonal antibody are useful in treating RSV. See the title and abstract and entire article.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a HMG-CoA reductase inhibitor in combination with an antibody composition in a method of inhibiting infection of a cell by a virus such as RSV.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a HMG-CoA reductase inhibitor in combination with an antibody composition, since a HMG-CoA reductase inhibitor is useful in inhibiting RSV as discussed above, and an antibody composition is known to be useful in treating RSV by inhibiting RSV. Therefore, one of ordinary skill in the art would have reasonably

expected that combining a HMG-CoA reductase inhibitor and an antibody composition, known useful for the same purpose, i.e., inhibiting a viral infection such as RSV, in a composition to be administered would improve the therapeutic effect for treating a viral infection such as RSV. Since all active composition components herein are known to useful to treat a viral infection such as RSV, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1229 submitted June 11, 2002) and Park et al. (C29, PTO-1229 submitted June 11, 2002) in view of Pastey et al. (C32, PTO-1229 submitted June 11, 2002) and Gruber et al. (C17, PTO-1229 submitted June 11, 2002)

The same teachings of Maziere et al. have been discussed above 103(a) rejection (see supra at page 5 of the instant Office Action).

The same teachings of Park et al. have been discussed above 103(a) rejection (see supra at page 5 of the instant Office Action).

The same teachings of Pastey et al. have been discussed above 103(a) rejection (see supra at page 6 of the instant Office Action).

The above cited prior art does not expressly disclose the employment of HMG-CoA reductase inhibitors in combination with ribavarin in a method of inhibiting infection of a cell by a virus such as RSV.

Gruber et al. teaches that ribavarin is useful in treating RSV. See the title and abstract and entire article.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a HMG-CoA reductase inhibitor in combination with ribavarin in a method of inhibiting infection of a cell by a virus such as RSV.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a HMG-CoA reductase inhibitor in combination with ribavarin, since a HMG-CoA reductase inhibitor is useful in inhibiting RSV as discussed above, and ribavarin is known to be useful in treating RSV by inhibiting RSV. Therefore, one of ordinary skill in the art would have reasonably expected that combining a HMG-CoA reductase inhibitor and ribavarin, known useful for the same purpose, i.e., inhibiting a viral infection such as RSV, in a composition to be administered would improve the therapeutic effect for treating a viral infection such as RSV. Since all active composition components herein are known to useful to treat a viral infection such as RSV, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
March 31, 2003